

Access DB# 136892**SEARCH REQUEST FORM****Scientific and Technical Information Center**

Requester's Full Name: Alton Ryan Examiner #: 74458 Date: 11/2/04  
Art Unit: 1616 Phone Number 302-20621 Serial Number: 101049821  
Mail Box and Bldg/Room Location: REN 4A39 Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_

Inventors (please provide full names): \_\_\_\_\_

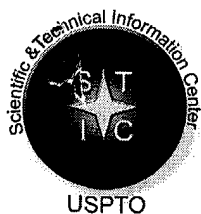
Earliest Priority Filing Date: \_\_\_\_\_

*\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Search: ~~1~~  
① Structure of claim 4  
② inflammatory or analgesic  
③ combine ① + ②

**STAFF USE ONLY**

	Type of Search	Vendors and cost where applicable
Searcher: <u>Skopman</u>	NA Sequence (#) _____	STN _____
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: <u>11/2/04</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____



# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 136892**

**TO: Alton Pryor  
Location: Rem 4A39  
Art Unit: 1616  
November 2, 2004**

**Case Serial Number: 10/049821**

**From: P. Sheppard  
Location: Remsen Building  
Phone: (571) 272-2529**

**sheppard@uspto.gov**

### **Search Notes**

=> fil hcaplus  
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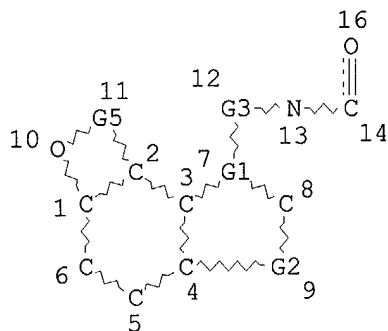
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FILE COVERS 1907 - 2 Nov 2004 VOL 141 ISS 19  
 FILE LAST UPDATED: 1 Nov 2004 (20041101/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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 L3 STR



VAR G1=C/N  
 VAR G2=C/N/O/S  
 REP G3=(1-4) C  
 REP G5=(2-4) A  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE  
 L4 92 SEA FILE=REGISTRY SSS FUL L3  
 L6 SEL PLU=ON L4 1- CHEM : 96 TERMS  
 L7 38 SEA FILE=HCAPLUS ABB=ON PLU=ON L6  
 L8 165853 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ANTI-INFLAMMATORY AGENTS"/CV  
 OR "INFLAMMATION INHIBITORS"/CV OR "INFLAMMATION INHIBITORS  
 AND ANTIARTHRITICS"/CV OR "ANTI-INFLAMMATORY DRUGS"/CV OR  
 "ANTI-INFLAMMATORY SUBSTANCES"/CV OR ANTIINFLAMMATANTS/CV OR

ANTIINFLAMMATORIES/CV OR ANTIPHLOGISTICS/CV OR ANTIARTHRITICS/CV OR "ANTIRHEUMATIC AGENTS"/CV OR MELITTIN/CV OR "INFLAMMATION INHIBITORS (L) ANTIARTHRITICS"/CV OR "INFLAMMATION INHIBITORS (L) ANTIARTHRITICS"/CV OR "INFLAMMATION INHIBITORS (L) NONSTEROIDAL"/CV OR "INFLAMMATION INHIBITORS (L) TOPICAL"/CV OR ANTIASTHMATICS/CV OR CORTICOSTEROIDS/CV OR INFECTION/CV OR INFLAMMATION/CV OR 1-TERT-BUTOXYCARBONYL-4-PIPERIDONE/CV OR "6-METHOXY-2-NAPHTHYLACETIC ACID"/CV OR "BECLOMETHASONE DIPROPIONATE"/CV OR CELECOXIB/CV OR CROMOLYN/CV OR DICLOFENAC/CV OR "DICLOFENAC SODIUM"/CV OR DIFLUNISAL/CV OR ETANERCEPT/CV OR "ETHYL 2-CHLOROACETOACETATE"/CV OR "ETHYL ISONIPECOTATE"/CV OR ETODOLAC/CV OR FENBUFEN/CV OR FENOPROFEN/CV OR KETOROLAC/CV OR "MECLOFENAMIC ACID"/CV OR "MEFENAMIC ACID"/CV OR MELOXICAM/CV OR "METHYLPREDNISOLONE SODIUM SUCCINATE"/CV OR "NS 398"/CV OR NABUMETONE/CV OR "NIFLUMIC ACID"/CV OR ROFECOXIB/CV OR SUPROFEN/CV OR TENOXICAM/CV OR TOLMETIN/CV OR TRIAMCINOLONE/CV OR "TRIAMCINOLONE ACETONIDE"/CV OR VALDECOXIB/CV OR VIDARABINE/CV)

L9 134932 SEA FILE=HCAPLUS ABB=ON PLU=ON ("NERVOUS SYSTEM AGENTS"/CV OR "NERVOUS SYSTEM DEPRESSANTS"/CV OR ANALGESICS/CV OR ANODYNES/CV OR "ANTINOCICEPTIVE AGENTS"/CV OR "ANTINOCICEPTIVE COMPOUNDS"/CV OR ANTINOCICEPTIVES/CV OR NARCOTICS/CV OR OPIATES/CV OR "OPIATES AND OPIOIDS"/CV OR OPIOIDS/CV OR BUTORPHANOL/CV OR ENKEPHALINS/CV OR "(D-PEN2, D-PEN5)ENKEPHALIN"/CV OR DADLE/CV OR "LEUCINE ENKEPHALIN"/CV OR "METHIONINE ENKEPHALIN"/CV OR PROENKEPHALIN/CV OR LOPERAMIDE/CV OR NALBUPHINE/CV OR "OPIUM ALKALOIDS"/CV OR ANALGESIA/CV OR ANESTHETICS/CV OR ANTIPYRETICS/CV OR "HYPNOTICS AND SEDATIVES"/CV OR PAIN/CV OR "PAIN RECEPTORS"/CV OR VANILLOIDS/CV OR ALFENTANIL/CV OR BUPIVACAINE/CV OR BUPRENORPHINE/CV OR CODEINE/CV OR DEXTROMETHORPHAN/CV OR DICLOFENAC/CV OR DIFLUNISAL/CV OR DIHYDROCODEINE/CV OR DIHYDROMORPHINE/CV OR FENTANYL/CV OR GABAPENTIN/CV OR HYDROCODONE/CV OR HYDROMORPHONE/CV OR KETOROLAC/CV OR MEPERIDINE/CV OR METAMIZOLE/CV OR MORPHINE/CV OR "MORPHINE SULFATE"/CV OR NEOSTIGMINE/CV OR OXYCODONE/CV OR REMIFENTANIL/CV OR ROPIVACAINE/CV OR SUFENTANIL/CV OR TRAMADOL/CV)

L10 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND (L8 OR L9)

=> d ibib abs kwic hitstr l10 1-6

L10 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2004:610036 HCAPLUS  
 DOCUMENT NUMBER: 141:145717  
 TITLE: Sedative non-benzodiazepine formulations  
 INVENTOR(S): O'Toole, Edel; Fogarty, Siobhan  
 PATENT ASSIGNEE(S): Biovail Laboratories Inc., Barbados  
 SOURCE: PCT Int. Appl., 67 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062564	A2	20040729	WO 2004-IB18	20040108
WO 2004062564	A3	20040910		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU,

ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ,  
KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN,  
MW, MX, MX, MZ

US 2003165566 A1 20030904 US 2003-338876 20030109  
PRIORITY APPLN. INFO.: US 2003-338876 A 20030109  
US 2002-346613P P 20020110

AB The invention provides for an enhanced absorption pharmaceutical composition comprising a plurality of microparticles, each microparticle comprising at least one sedative non-benzodiazepine, at least one spheronization aid and at least one solubility enhancer. The microparticles of the invention are further incorporated into an oral fast-dispersing dosage form.

IT Human

**Hypnotics and Sedatives**

Insomnia

Particle size distribution

Solubilizers

Spheronization

(sedative non-benzodiazepine formulations)

IT 50-70-4, Sorbitol, biological studies 60-87-7, Promethazine 87-99-0, Xylitol 113-18-8, Ethchlorvynol 151-21-3, Sodium lauryl sulfate, biological studies 302-17-0, Chloral hydrate 533-45-9, Clomethiazole 2218-68-0, Chloral betaine 9003-39-8, Polyvinylpyrrolidone 9005-65-6, Tween 80 18641-57-1, Glyceryl behenate 19794-93-5, Trazodone 25322-68-3D, ethers 43200-80-2, Zopiclone 82626-48-0, Zolpidem 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 121548-04-7, Gelucire 44/14 121548-05-8, Gelucire 50/13 138729-47-2, Esopiclone 151319-34-5, Zaleplon 162883-07-0, Ccd-3693 **196597-26-9**, **TAK-375** 325715-02-4, Indiplon 565462-01-3, Co-32693 565462-02-4, Ip-100-9 565462-03-5, Pprt-211 727733-43-9, SC 72393  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(sedative non-benzodiazepine formulations)

IT **196597-26-9**, **TAK-375**

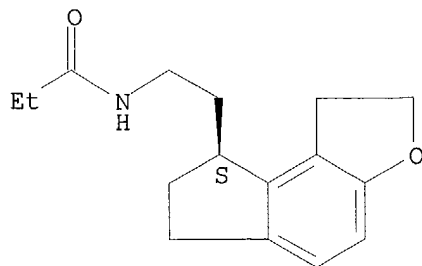
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(sedative non-benzodiazepine formulations)

RN 196597-26-9 HCAPLUS

CN Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:197432 HCAPLUS

DOCUMENT NUMBER: 140:296697

TITLE: **TAK-375**: treatment of insomnia  
treatment of circadian rhythm disorders melatonin  
MT1/MT2 agonist

AUTHOR(S): Chilman-Blair, K.; Castaner, J.; Silvestre, J. S.;  
 Bayes, M.  
 CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain  
 SOURCE: Drugs of the Future (2003), 28(10), 950-958  
 CODEN: DRFUD4; ISSN: 0377-8282  
 PUBLISHER: Prous Science  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English

AB A review. Melatonin is a neurohormone produced in the pineal gland that is involved in the regulation of circadian rhythm function. It works through activation of its intrinsic receptors found in the suprachiasmatic nucleus (SCN) within the hypothalamus. Melatonin synthesis is under direct neural control from SCN firing. The sleep/wake cycle is a circadian rhythm controlled by this neural complex. Problems in the functioning of this system can therefore lead to sleep disorders. While melatonin itself has been shown to be effective in the treatment of sleep disorders, problems due to its ubiquitous action in the brain have limited its use for this indication. **TAK-375** is a potent melatonin receptor agonist, specific for the ML1 receptor subtype known to be intricately involved in circadian rhythm function. **TAK-375** has been heralded as an exciting new drug candidate for the treatment of patients with insomnia and circadian rhythm dysfunction. Phase III trials are currently under way to test the drug's viability for use in patients with sleep disorders.

TI **TAK-375: treatment of insomnia.** . . .

AB . . . for this indication. **TAK-375** is a potent. . .  
 . circadian rhythm function. **TAK-375** has been  
 heralded. . .

IT Sleep  
 (-waking cycle; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm disorders)

IT Rhythm, biological  
 (circadian, regulation of; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm  
 disorders)

IT Sleep  
 (disorder; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm disorders)

IT Aging, animal  
 (elderly; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm disorders)

IT Brain  
 (hypothalamus, suprachiasmatic nucleus; melatonin MT1/MT2 agonist  
**TAK-375** treatment of patients with insomnia and  
 circadian rhythm disorders)

IT Human  
**Hypnotics and Sedatives**  
 Insomnia  
 Pineal gland  
 (melatonin MT1/MT2 agonist **TAK-375** treatment of  
 patients with insomnia and circadian rhythm disorders)

IT Neurohormones  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (melatonin MT1/MT2 agonist **TAK-375** treatment of  
 patients with insomnia and circadian rhythm disorders)

IT Melatonin receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (type MT1, agonist; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm disorders)

IT Melatonin receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (type MT2, agonist; melatonin MT1/MT2 agonist **TAK-375**  
 treatment of patients with insomnia and circadian rhythm disorders)

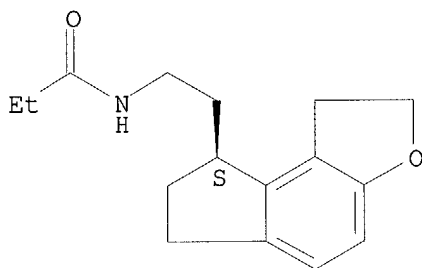
IT **196597-26-9P, TAK-375**  
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (melatonin MT1/MT2 agonist **TAK-375** treatment of patients with insomnia and circadian rhythm disorders)

IT 73-31-4, Melatonin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (melatonin MT1/MT2 agonist **TAK-375** treatment of patients with insomnia and circadian rhythm disorders)

IT **196597-26-9P, TAK-375**  
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (melatonin MT1/MT2 agonist **TAK-375** treatment of patients with insomnia and circadian rhythm disorders)

RN 196597-26-9 HCAPLUS  
 CN Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2003:897579 HCAPLUS  
 DOCUMENT NUMBER: 140:296592  
 TITLE: Recent progress of hypnotic drug therapy  
 AUTHOR(S): Nakajima, Toru; Sugano, Michi  
 CORPORATE SOURCE: School of Medicine, Kyorin University, Japan  
 SOURCE: Gendai Iryo (2003), 35(10), 2439-2446  
 CODEN: GEIRDK; ISSN: 0533-7259  
 PUBLISHER: Gendai Iryosha  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: Japanese

AB A review. The history and characteristic of hypnotic drugs including  
 ol selectivity, the influence of hypnotic drugs on the different  
 sleeping stages, the metabolism of hypnotic drugs, and recent development of  
 hypnotic drugs such as **TAK-375** etc. is reviewed.

AB . . . drugs such as **TAK-375** etc. is reviewed.

IT **Hypnotics and Sedatives**  
 (recent progress of hypnotic drug therapy)

IT **196597-26-9, TAK-375**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (recent progress of hypnotic drug therapy)

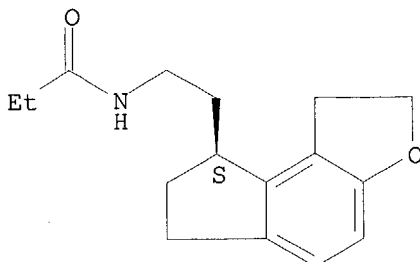
IT **196597-26-9, TAK-375**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
(recent progress of hypnotic drug therapy)

RN 196597-26-9 HCAPLUS

CN Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2003:570816 HCAPLUS  
 DOCUMENT NUMBER: 139:138735  
 TITLE: Sedative non-benzodiazepine formulations  
 INVENTOR(S): O'Toole, Edel; Fogarty, Siobhan  
 PATENT ASSIGNEE(S): Biovail Laboratories Inc., Barbados  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059349	A1	20030724	WO 2003-IE1	20030109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1469848	A1	20041027	EP 2003-729537	20030109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			US 2002-346613P	P 20020110
			WO 2003-IE1	W 20030109
AB The invention provides for an enhanced absorption pharmaceutical composition comprising a plurality of microparticles, each microparticle comprising at least one sedative non-benzodiazepine, at least one spheronisation aid, and at least one solubility enhancer. The microparticles of the invention are further incorporated into an oral fast-dispersing dosage form. For example, microparticles were prepared containing zolpidem tartrate 15%, Gelucire 50/13 35%, and distilled monoglyceride (Myvaplex) 50%. Microparticles obtained were then coated for taste masking with a coating solution containing a 60:30:10 ratio of Eudragit NE30D, talc, and Methocel. The coated microparticles were used for preparation of tablets.				
IT Dissolution				



Drug bioavailability

**Hypnotics and Sedatives**

Solubilizers

(preparation of microparticles for enhanced oral bioavailability of non-benzodiazepine sedatives)

IT 60-87-7, Promethazine 113-18-8, Ethchlorvynol 302-17-0, Chloral hydrate 533-45-9, Clomethiazole 2218-68-0, Chloral betaine 19794-93-5, Trazodone 43200-80-2, Zopiclone 82626-48-0, Zolpidem 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 99294-93-6, Zolpidem tartrate 138729-47-2, Esopiclone 151319-34-5, Zaleplon 162883-07-0, CCD 3693 **196597-26-9, TAK 375** 325715-02-4, Indiplon 565462-01-3, Co 32693 565462-02-4, IP 100-9 565462-03-5, PPRT 211

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of microparticles for enhanced oral bioavailability of non-benzodiazepine sedatives)

IT **196597-26-9, TAK 375**

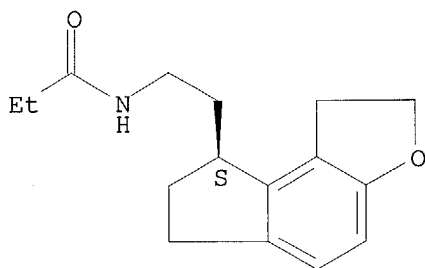
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of microparticles for enhanced oral bioavailability of non-benzodiazepine sedatives)

RN 196597-26-9 HCAPLUS

CN Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:167841 HCAPLUS

DOCUMENT NUMBER: 134:212749

TITLE: Matrix adhering to nasal mucosa

INVENTOR(S): Akiyama, Yoko; Nagahara, Naoki; Bando, Hiroto

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

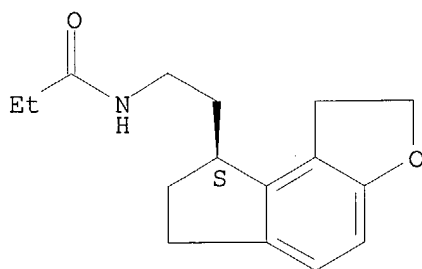
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015735	A1	20010308	WO 2000-JP5739	20000825
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ,				

BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 JP 2001131057 A2 20010515 JP 2000-255493 20000825  
 EP 1206943 A1 20020522 EP 2000-991043 20000825  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL  
 US 6663883 B1 20031216 US 2002-69072 20020221  
 PRIORITY APPLN. INFO.: JP 1999-240162 A 19990826  
 WO 2000-JP5739 W 20000825  
 OTHER SOURCE(S): MARPAT 134:212749  
 AB Disclosed is a matrix adhering to the nasal mucosa which allows improved  
 transfer into the brain of a drug exerting its effect in the brain and is  
 capable of continuously supplying the drug into the brain. This matrix  
 contains a polyglycerol fatty acid ester, the drug exerting its effect in  
 the brain, and a sticky substance. Polyglycerol docosanoate (HB 310) and  
 hydrogenated castor oil were heated. To the above mixture, cephalexin and  
 Hiviswako 104 were added and the resulting mixture was made into granules.  
 IT Antidepressants  
 Brain  
 Drug bioavailability  
**Hypnotics and Sedatives**  
 Tranquilizers  
 (matrix adhering to nasal mucosa for improved drug transfer to brain)  
 IT 9004-64-2, Hydroxypropyl cellulose 15686-71-2, Cephalexin 25618-55-7D,  
 Polyglycerin, fatty acid esters 64366-79-6, HB 310 89286-85-1,  
 Hiviswako 104 162874-49-9, Kadoran **196597-26-9**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (matrix adhering to nasal mucosa for improved drug transfer to brain)  
 IT **196597-26-9**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (matrix adhering to nasal mucosa for improved drug transfer to brain)  
 RN 196597-26-9 HCAPLUS  
 CN Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-  
 yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

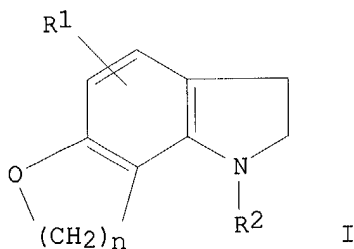


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1995:943453 HCAPLUS  
 DOCUMENT NUMBER: 123:340087  
 TITLE: Preparation of indolines which are melatonin receptor  
 agonists and antagonists  
 INVENTOR(S): North, Peter Charles; Carter, Malcolm Clive  
 PATENT ASSIGNEE(S): Glaxo Group Ltd., UK  
 SOURCE: PCT Int. Appl., 42 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9517405	A1	19950629	WO 1994-EP4220	19941220
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9410056	A	19951018	ZA 1994-10056	19941219
CA 2179402	AA	19950629	CA 1994-2179402	19941220
AU 9512743	A1	19950710	AU 1995-12743	19941220
AU 684877	B2	19980108		
EP 736028	A1	19961009	EP 1995-903817	19941220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
IL 112097	A1	19980615	IL 1994-112097	19941221
US 5633276	A	19970527	US 1996-652460	19960614
PRIORITY APPLN. INFO.:			GB 1993-26192	19931222
			WO 1994-EP4220	19941220
OTHER SOURCE(S):		MARPAT 123:340087		
GI				



AB The title compds. [I; R1 = H, halogen, C1-6 alkyl; R2 = CR3R4(CH2)pNR5COR6; R3-R5 = H, C1-6 alkyl; R6 = C1-6 alkyl, C3-7 cycloalkyl; p = 1-4; n = 2-4], useful as melatonin receptor agonists and antagonists in the treatment of conditions associated with a disturbed functioning of the melatonin system [i.e., jet lag (no data), osteoporosis (no data), CNS disorders (no data), etc. (no data)], are prepared and I-containing formulations presented. Thus, 2-(5-chloro-2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethylamine was amidated with Ac2O, producing N-[2-(5-chloro-2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethyl]acetamide, m.p. 147-149°, which demonstrated a IC50 against the binding of melatonin to rabbit retina of 0.004 nM.

IT **Nervous system agents**

(indolines which are melatonin receptor agonists and antagonists)

IT **170728-91-3P 170728-92-4P 170729-12-1P**

**170729-13-2P 170729-14-3P 170729-15-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indolines which are melatonin receptor agonists and antagonists)

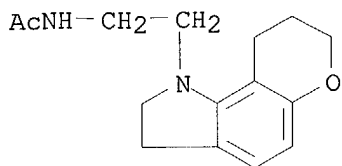
IT **170728-91-3P 170728-92-4P 170729-12-1P**

**170729-13-2P 170729-14-3P 170729-15-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of indolines which are melatonin receptor agonists and antagonists)

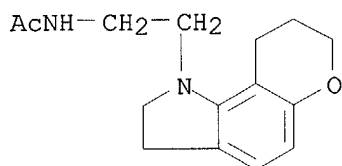
RN 170728-91-3 HCAPLUS

CN Acetamide, N-[2-(2,3,8,9-tetrahydropyrano[2,3-g]indol-1(7H)-yl)ethyl]-  
(9CI) (CA INDEX NAME)



RN 170728-92-4 HCAPLUS

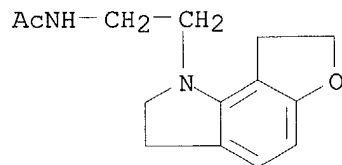
CN Acetamide, N-[2-(2,3,8,9-tetrahydropyrano[2,3-g]indol-1(7H)-yl)ethyl]-,  
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

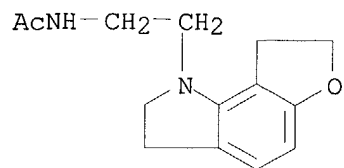
RN 170729-12-1 HCAPLUS

CN Acetamide, N-[2-(2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethyl]- (9CI)  
(CA INDEX NAME)



RN 170729-13-2 HCAPLUS

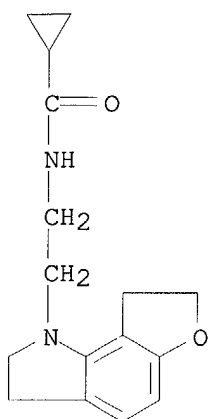
CN Acetamide, N-[2-(2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethyl]-,  
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

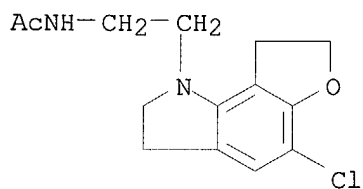
RN 170729-14-3 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-(2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 170729-15-4 HCAPLUS

CN Acetamide, N-[2-(5-chloro-2,3,7,8-tetrahydro-1H-furo[2,3-g]indol-1-yl)ethyl]- (9CI) (CA INDEX NAME)



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